Remarks

Claims 127-132 are pending. Claims 127 and 128 are newly amended, without prejudice to subsequent prosecution of the cancelled subject matter . No new matter has been entered.

Claims rejections – 102(e)

Claims 127-132 are rejected under 102(e) as being anticipated by Cao *et al.* (U.S. Patent application publication US2005/0084850.

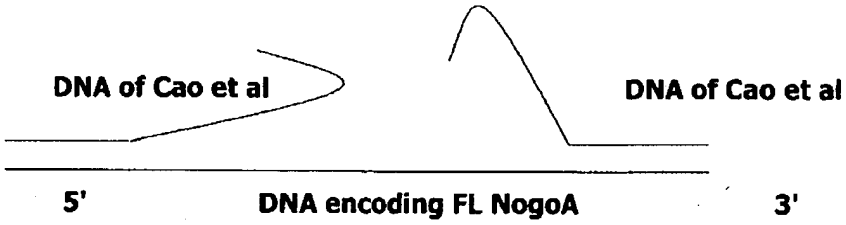
Applicant respectfully traverses on the grounds that Cao *et al.* does not teach every limitation of the claims.

Cao *et al.* discloses a number of cDNA sequences obtained from bone marrow stromal cells. From these cDNA sequences, the authors predict the translated amino acid sequence(s). An alignment of the protein sequence of SEQ ID NO:6 (encoded by cDNA sequence of SEQ ID NO:5) of Cao *et al.* with SEQ ID NO:29 of this application is provided by Applicant. See Annex 1, attached herewith.

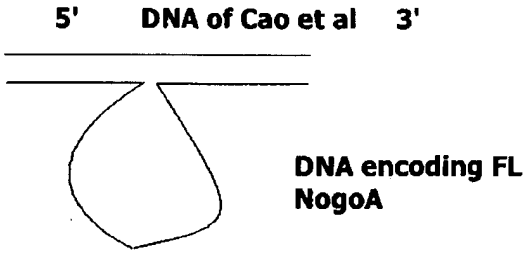
Claim 127 is drawn to an isolated nucleic acid comprising a polynucleotide which hybridizes under high stringency conditions to, and along the entire length of, a second nucleic acid which consists of a nucleotide which encodes the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO:29.

According to the Examiner, the cDNA sequence of SEQ ID NO:5 taught by Cao *et al.* would hybridize under high stringent conditions with a nucleotide encoding the polypeptides defined in claim 127. However, the Examiner has provided no proof or indication that such a fragment would be able to hybridize to the sequence encoding the full-length rat or human Nogo protein as indicated by SEQ ID NO: 2 and 29, respectively. Applicant contends it is highly unlikely that a fragment of about 1000 nucleotides encompassing the start and the end of the normal cDNA sequence having 3400 nucleotides, would be found to hybridize under stringent conditions due to the presence of a gap of over 2000 nucleotides between the Cao *et al.* sequence of SEQ ID NO:5 and either of Applicant's sequences of SEQ ID NO: 2 and 29.

The following would happen: either the Cao *et al.* cDNA molecule binds either to the 3' end or to the 5' end of the nucleotide encoding the full-length (FL) Nogo A protein, in both case leaving a stretch of over 1500 nucleotides unbound. The resulting gap in hybridization is inconsistent with the Cao *et al.* cDNA molecule's hybridizing under the instantly recited stringent conditions over the full length of SEQ ID NO:2 or SEQ ID NO:29 as required by claim 127 as newly amended.



Alternatively, if the Cao *et al.* DNA would bind both the 3' end and the 5' end of the nucleotide encoding the full-length Nogo A protein at the same time, the latter would have to be folded up in the middle, leaving an enormous loop of 2000 nucleotides somewhere in the middle of the hybrid DNA molecule. Again, the resulting gap in hybridization is inconsistent with the Cao *et al.* cDNA molecule's hybridizing under the instantly recited stringent conditions over the full length of SEQ ID NO:2 or SEQ ID NO:29 as required by claim 127 as newly amended.



In addition to newly amending claim 127 to indicate that the claimed polynucleotide hybridizes along the full length of SEQ ID NO:29 or SEQ ID NO:2, Applicant has also deleted the previously recited fusion proteins from claim 127, solely in the interest of advancing prosecution, and without prejudice to cancelled subject material. In view of these amendments, Applicant respectfully submits that the nucleotide sequence of Cao *et al.* does not anticipate the isolated nucleic acid of claim 127, since the nucleotide sequence of Cao *et al.* does not have the potential to hybridize under stringent conditions over the full length of SEQ ID NO:29 or SEQ ID NO:2 which encode the Nogo A protein.

Claims 128-132

According to the Examiner, SEQ ID NO:5 of the Cao *et al.* application represents a cDNA sequence encoding a protein that has 99.1% identity to the human Nogo A protein sequence as instantly claimed in claims 128-132. Applicant does not agree with this view for the following reasons:

SEQ ID NO:6 of the Cao *et al.* patent application publication presents the predicted amino acid sequence of SEQ ID NO:5, which corresponds to the human Nogo A SEQ ID NO: 29 only in amino acids 1-185. The remaining predicted amino acid sequence is completely different from the human Nogo A sequence of SEQ ID NO:29. There is nothing in the published application of Cao *et al.* that indicates that the protein sequence may have been predicted in an erroneous manner, let alone that there is any guidance as to how the correctly predicted protein sequence should look like. There are always six possible reading frames deducible from a single cDNA sequence; +1, +2, +3 and -1, -2 and -3, depending on the direction the codons are read and from which nucleotide the codons are defined. Only one of these six frames results in the correct translation of the protein encoded thereby, in this case the human Nogo A protein. The published application of Cao *et al.* does not predict the protein sequence of Nogo A correctly in that the reading frame is somehow shifted at position 185 of the amino acid sequence in SEQ ID NO 6. Please see Applicant's alignment of the protein sequence of SEQ ID NO:6 (encoded by cDNA sequence of SEQ ID NO:5) of Cao *et al.* with SEQ ID NO:29 of this application. Annex 1, attached herewith.

Accordingly, the predicted amino acid sequence of Cao *et al.*, does not anticipate the subject-matter of instant claims 128-132. Even though it may be possible to deduce the correct amino acid sequence from the cDNA sequence in SEQ ID NO:5 of Cao *et al.*, this would have to be done using hindsight, since multiple protein sequences would have to be analyzed for their putative correctness. Before the priority date of the NIAG-OO1 application, there was no information available about the protein sequence of the human Nogo A. It would therefore also be impossible for the skilled person to choose the correct Nogo A protein sequence from the three possible amino acid frames, since there is no guidance in the Cao *et al.* publication, nor in the remaining prior art, of how to do this in a correct manner. Only with hindsight of knowing the exact amino acid sequence of the human Nogo A as provided by the Applicant's instant patent application would it be possible to deduce the correct protein sequence as defined by SEQ ID NO:2 or 29.

Applicant has deleted the recitation of the fusion protein that completely overlaps instant SEQ ID NO:29, i.e., amino acids 1-172 fused to the 188 C-terminal amino acids of SEQ ID NO:29, from claims 128-131. The remaining recited fusion protein that only partly overlaps SEQ ID NO:2, i.e., amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO:2, is novel for the same reasons as detailed above for the full-length sequences of SEQ ID NO:2 and 29.

Conclusion

In view of Applicant's amendments limiting the subject-matter of claim 127 to an isolated nucleic acid comprising a polynucleotide which hybridizes under high stringency conditions to, and along the entire length of, a second nucleic acid which consists of a nucleotide which encodes the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO:29, encoding the full-length rat or human Nogo A protein, and the deletion of the recitation of the nucleic acid encoding the fusion protein of amino acids 1-171 to the C-terminal 188 amino acids of SEQ NO: 29, Applicant submits that the subject-matter of the instant claims is both new and non-obvious over the disclosure of Cao *et al.* Reconsideration and withdrawal of the instant rejection is respectfully requested.

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with

Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Respectfully submitted,

Date: October 23, 2008

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